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The four most commonly recognized systems protecting "intellectual property" are trademark, patent, trade secret and copyright. Trademark law is easily distinguished and offers little opportunity for a firm to protect its work product. Thus, this paper will address only the remaining options. Generally, sorting among them is fairly straightforward.

Copyright

As its name implies, copyright is designed to protect its holder against copying by others. It has a defined term for covered works such as paintings and musical compositions. However, the protection is said to extend to the expression of ideas not to ideas themselves. Functionality is the enemy of copyright. If an idea can be expressed in only one (or a few) ways, the possibility of copyright protection is significantly weakened.

The only potential for copyright in protecting biotechnology relates to a suggestion that DNA sequences (and I suppose amino acid sequences) might be protected the way that software is.[1] Yet, probably because copyright protects only against copying and not against independent discovery, this suggestion appears to have gotten lost in the rush to patent genes. It may be useful to dust it off again in

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1 Irving Kayton, *Copyright in Living Genetically Engineered Works,* 50 Geo. Wash. L.Rev. 191 (1982).

light of the current flurry to sequence large numbers of DNA molecules obtained from expression libraries.

The patent application filed by the NIH claiming "expression sequence tags" (ESTs) retrieved and sequenced by Dr. Craig Venter and Dr. Mark Adams has received wide publicity. Inspired, presumably, by the attempt to sequence the entire human genome, and recognizing the fact that approximately 99% of the human genomic DNA does not encode any proteins, Venter and Adams set about obtaining DNA sequences by reverse transcribing the messenger RNA found in brain cells. Because the messenger RNA embodies only genes on their way to becoming proteins, the 99% nonsense sequences are automatically eliminated, and the sequenced material is putatively derived from the 1% of the genome that encodes protein (and its associated translation regulating elements). Thus, Venter and Adams were able to retrieve and sequence this reverse transcribed cDNA with astonishing efficiency, and the initial NIH application contained approximately 300 sequenced ESTs.

The number has now grown to many thousands; Drs. Venter and Adams have left the NIH and continue their work in a private institute. In the meantime, other companies such as Incyte Pharmaceuticals in Palo Alto, California and a Japanese company, and probably others, have entered the race to obtain sequences associated with the estimated approximately 100,000 genes embedded among all the nonsense in the human genome. The hue and cry raised by the prospect of protecting so many DNA sequences by patent has resulted in a proposal to place a two-year moratorium on patents related to the human genome (a proposal that was not enacted) and in a study by the Office of Technology Assessment on the implications of this work.

To the extent that ESTs represent copyrightable expressions, this might prevent others from "stealing" sequencing work already done[2] but would not prevent the use of independently recovered forms of the

2 The question is not only whether the subject matter is "functional," as mentioned above, but also whether it merely comprises data. The Supreme Court recently held that copyright does not protect data from copying, much less independent origin; Feist v. Rural Telephone Service, Inc., 111 S.Ct. 1282 (1991).

relevant genes and ESTs. Because copyright arises automatically upon fixing an expression in a tangible form, whatever protection is available already exists.[3] Aside from this possibility, however, copyright protection as applied to biotechnology is not particularly exciting.

Patents

Although the property is said to be intangible, patent protection is considered an asset of the patent holder. Quite often, patents are the only assets of a young company grounded in a high technology endeavor and requiring large R&D expenditure prior to marketing any product at all. Therefore, obtaining an appropriate patent portfolio is an important instrument in attracting investment and assuring investors that when products and services are finally marketed, exclusivity will be assured to the company.

The patent system is established in the U.S. (and in other jurisdictions) by statute. Title 35 of the U.S. Code provides a 17-year term during which the patentee may *exclude others* from making, using or selling the claimed subject matter in the U.S. It is worth noting that patentees may be prevented from practicing their own inventions by patents held by others.

The 17-year monopoly is considered a quid pro quo for full disclosure of the invention to the public. This disclosure is made through an application filed with the U.S. Patent and Trademark Office (PTO) which is required to "contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."[4]

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3 Copyright notice is no longer necessary to maintain protection in published works, and registration is unnecessary unless one wants to bring an action. *See, e.g.*, 17 U.S.C. § 411.

4 35 U.S.C. § 112, ¶ 1.

Applications that fail to comply with this section of the statute cannot form the basis for the grant of a patent as defined by the claims included in the application. The claims have to be directed to a composition of matter, a process, a machine, or an article of manufacture.[5] Of course, the subject matter does not have to be claimed in those terms. It is simply to be claimed in such a way that the claims particularly point out and distinctly claim the subject matter which the applicant regards as his invention.[6] Claims of relevance in biotechnology can be directed to proteins, DNA molecules, cells, mice, antibodies, methods of treatment, methods of recombinant production, oligosaccharides, oligonucleotides and so forth. They can also be directed to assay devices, chromatographic columns, methods to conduct electrophoresis, panels of peptides, and methods of diagnosis. All of the foregoing are, if properly claimed, "statutory subject matter."[7]

The subject matter of successful claims must meet other criteria: It must be new, useful, and nonobvious. The novelty requirement is the least troublesome; the claimed subject matter simply must not have existed somewhere in the form in which it is claimed. In the context of biotechnology, the most obvious concern is the patentability of natural products, which, at first glance, appear to have preexisted. This is true only up to a point, and the precedent is well established that if these materials can be claimed in a manner which distinguishes them from their status as they occur in nature, there is no barrier to patentability. Early cases, prebiotech revolution, set the groundwork for this where prostaglandins and vitamin B_{12}, when claimed as pure compounds, were considered distinguishable from the gemishes in which they were originally found. Similarly, patents have now issued on DNA encoding erythropoietin, pure TPA, DNA encoding TPA, and so forth. There is no longer any question that the existence of the essential features of the

5 35 U.S.C. § 101.

6 35 U.S.C. § 112, ¶2.

7 Not all of these are statutory subject matter in every country. Methods of treatment, for example, are unpatentable in most jurisdictions. What will and will not be included, as is the case with most legal provisions, is basically a political decision.

claimed subject matter in a natural state is not a barrier to patentability in properly constructed claims.

The Utility Requirement

Claimed inventions must be "useful".[8] There doesn't seem to be any question that if, for example, a compound can be shown to kill weeds, or to reduce inflammation, or to cure an infection, it is useful to the general consuming public. It also seems clear that if a compound is useful as a laboratory reagent, for example as a dye to detect the presence of a protein on a chromatogram, it is useful to the research community. It is also clear that if a compound is "useful" only to find out what it is good for, that "utility" is not sufficient.

A related question relates to the level of proof required to demonstrate that the utility asserted for a claimed method or compound is in fact accurate. It is clear, in the context of applying for patent protection, that the burden is on the examiner to show that the asserted utility is not credible.[9]This burden is not particularly great, apparently, depending on what the asserted utility is and how the PTO chooses to treat it.

The putatively controlling case on questions of utility is Brenner v. Manson.[10] Manson, the applicant, invented a process for making a steroid that was a homolog of another steroid with tumor inhibiting effects in mice. After filing, probably in response to a PTO rejection, Manson submitted an article from the **Journal of Organic Chemistry** describing the class of steroids to which the one prepared by his process belonged. Some members of the class had antitumor activity, but the Court held that this was inadequate to show that the steroid prepared by the claimed process would also have such an effect. Because the intended product was not otherwise shown to be useful, the Court held the process to produce it wasn't useful.

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8 35 U.S.C. § 101.

9 In re Langer, 183 U.S.P.Q. 288 (CCPA 1974); In re Marzocchi, 169 U.S.P.Q. 367 (CCPA 1971).

10 383 U.S. 519 (1966).

The Court evidently wanted to stem what it perceived as a tide toward requiring no statement or showing of utility at all. Earlier, the Court of Customs Patent Appeals (CCPA) had reversed a rejection, for lack of utility, of a claim to steroid intermediates, where the steroids that would be produced from them had no disclosed utilities.[11] Also, the CCPA had held in *Manson* that utility should be found if a claimed process results in its intended product and its product is not detrimental to the public interest.[12] However, the Supreme Court, after addressing policy considerations, reversed, finally stating, "Unless and until a process is refined and developed to this point — where specific benefit exists in currently available form — there is insufficient justification for permitting an applicant to engross (sic) what may prove to be a broad field."

The implications of this decision are really quite unclear, beyond the simple statement that, "it is insufficient to meet the utility requirement to show that a claimed process successfully produces its intended product when there is no specified or known use for the intended product," the waters are murky. The case does not directly address the standard of proof required for establishing the asserted utility. It does hold that in the context of its facts, extrapolation from homologous compounds is not enough. But it is totally silent as to whether *in vitro* or *in vivo* tests are needed to establish therapeutic utility of a steroid or other compounds. It does not address the question of whether adequate utility would have been found had the applicant asserted, for example, that the steroid was useful as a control standard in a diagnostic assay for steroids in general. Perhaps if Manson had not been misled by the trend in the CCPA away from requiring an assertion of utility, a utility could have been asserted in his application that would have passed muster.

It is the element of adequate proof of therapeutic utility that causes the most problems for applicants attempting to protect biotechnology inventions. It is not as if the applicant does not know what kind of

11 In re Nelson, 126 U.S.P.Q. 242 (CCPA 1960).

12 In re Manson, 142 U.S.P.Q. 35 (CCPA 1964).

therapeutic utility the invention will have. It is rather that the PTO often demands levels of proof that are too expensive or too time consuming for applicants to assemble prior to the application for patent or even during the prosecution thereof. For example, in Ex parte Balzarini,[13] the Board upheld a rejection of claims directed to a pharmaceutical composition asserted to be effective to treat retroviral diseases in an animal or patient. The specification only contained *in vitro* tests. The Board held that these tests were not adequate proof of *in vivo* efficacy.

This approach by the PTO appears quite common, especially in claims to compositions asserted to be effective as vaccines, as antivirals, as antitumor agents, and the like. It is not clear why this is so, since therapeutic protocols which fail to work are applied every day in every hospital in the country. The protocols are evidently considered useful although manifestly they do not work, certainly not in every case or even in a substantial number of cases. Nevertheless, the PTO has consistently questioned assertions of such therapeutic utility — almost invariably, if the claims themselves are directed to methods of treatment and quite often if the therapeutic utility is the only use disclosed for a claimed composition of matter.

The dilemma faced by an applicant seeking to develop a new therapeutic compound is often resolved by disclosing, in addition to the real purpose for which the invention is intended, a "safe" utility that can be established without question. Such a "safe" utility might be that suggested for Manson's steroid above — as a control in a quantitative assay for steroids in general. A compound thought to be toxic to cancer cells might be useful in a screening method for cancer cell growth factors that overcome the effect of the toxin. A DNA molecule might be considered useful as a reagent to prime DNA synthesis in a controlled manner in the production of specifically binding DNA from mixtures. Sometimes construction of these "safe" utilities works. Sometimes the PTO won't buy it.

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13 21 U.S.P.Q.2d 1892 (BPAI 1992).

For example, in Ex parte Kranz,[14] the Board itself issued a rejection based on lack of utility to claims that were directed to a process for making a targeted cell susceptible to lysis by a cytotoxic T-lymphocyte. The claim itself did not require *in vivo* application of the technique; the claims were worded so as to cover laboratory procedures. But the Board said that the appellant's specification and brief "clearly indicate that the claimed process has as its practical objective a use *in vivo* specifically against cancer cells as the targets." So the Board issued a rejection, based on asserted inadequate proof of efficacy, of a method that was not even being claimed!

The question of patentable utility has been raised repeatedly in connection with the multiplicity of ESTs recently sought to be patented by the National Institutes of Health. Most are not associated with genes encoding proteins whose functions are known. Various utilities have been asserted including the use of the ESTs for chromosome mapping and as probes to retrieve genes which purportedly encode proteins that have some function since the genes are expressed in real tissues. The issue in this context is still unresolved.

I am unaware of recent court decisions relating to proof of therapeutic utility; but the Board of Patent Appeals and Interferences has fairly consistently upheld rejections where the examiner has asserted insufficient evidence to support a stated utility.[15] An exception is Ex parte Rubin[16] where claims were to a method for improving the effectiveness of interferon in the treatment of neoplastic conditions by administering an agent for inhibiting tyrosinase. The application provided *in vitro* tests which showed that tyrosinase denatured interferon, a known antitumor agent. The Board held that the utility described was not inherently incredible and that factual evidence was required if the claims were to be rejected on this basis.

14 19 U.S.P.Q.2d 1216 (BPAI 1990).

15 *See* Ex parte Busse, 1 U.S.P.Q.2d 1908 (BPAI 1986); Ex parte Rubin, 5 U.S.P.Q.2d 1461 (BPAI 1987); Ex parte Maas, 9 U.S.P.Q.2d 1746 (BPAI 1987); Ex parte Stevens, 16 U.S.P.Q.2d 1379 (BPAI 1990) and Ex parte Sudilovsky, 21 U.S.P.Q.2d 1702 (BPAI 1992).

16 5 U.S.P.Q.2d 1461 (BPAI 1987).

International Aspects

The economy is global, but patents are territorial. They do not provide exclusivity beyond the borders of the jurisdiction in which patents issue. The only arguably "long-arm" provision of the U.S. statute relates to pure process claims.[17] Since 1988, it has been an act of infringement to import or sell a product made by a process protected by a U.S. patent claim.[18] One reason it was added to the statute is that other jurisdictions have long followed this principle.

The significance of such protection for biotechnology is quite well known. Initial attempts, using these provisions, by Amgen to prevent importation of erythropoietin made with their patented DNA and cells were rebuffed. Since the claims in the Amgen patent had to do only with the materials for manufacture of erythropoietin, and not a process for its manufacture, they were considered not to be in a category that permitted the exclusion of the gene product.

Although it is recognized that much time and money could be saved with a uniform patent system at least covering the industrialized countries, a harmonization of existing patent systems is proving difficult, not to mention providing an independent mechanism for an international patent. European nations have taken a first step in the form of the European Patent Convention which went into force in 1978 and which provides a common examination and granting procedure for its 14 member countries. However, the grant of a European patent results only in a "bundle" of national patents which must be enforced on a country-by-country basis. The members of the convention intended to provide an alternative of a "community patent" in the last year but failed to do so.

An additional step has been the implementation of a Patent Cooperation Treaty that provides for a common application to be filed

17 There is also a type of product claim known as "product-by-process." Even before 1988, it was possible to exclude from importation such a *product* if made abroad by the claimed *process. See, e.g.,* Michael H. Dickman, *Commentary: Product-by-Process Claims in the U.S. Patent Practice,* 28 Idea 59 (1987).

18 *See* 35 U.S.C. §§ 271(g), 287(b) and 295.

applicable to all member countries (which include most of the jurisdictions important to biotechnology applicants). However, the examination procedure conducted in connection with this international application is nonbinding on jurisdictions in which the corresponding patent is eventually filed.

A major hurdle in any attempts at internationalization has been U.S. refusal to conform its patent system to those of almost all other jurisdictions in several important respects. First, the U.S. awards the patent to the first inventor of the claimed subject matter; everywhere else except the Philippines it is awarded to the first to file an application for claimed subject matter. It should be noted that in no jurisdiction is a noninventor entitled to a patent. Copying someone else's invention and filing the copied subject matter in the PTO is nowhere countenanced. Second, the U.S. patent term runs from the date of issue; everywhere else it runs from the date of filing. This has the effect of permitting the applicant for patent to time the period of the monopoly awarded at the patentee's convenience. Third, the U.S. keeps applications in confidence until the patent issues; everywhere else, applications are published eighteen months from the initial priority filing date. This last distinction is perhaps unimportant since participants in the global economy who file elsewhere realize that their applications will be published regardless of what the U.S. does.

Shop Rights

A shop right issue sometimes arises in the patent context but has nothing to do with the nature of protection afforded, the subject matter that can be protected or criteria for protectability. It has to do with what does and does not constitute infringement of an issued patent — i.e., whether certain entities may or may not be among those excluded from making, using and selling the claimed invention.

The issue arises when an employer fails to acquire ownership of the invented subject matter from an employed inventor. It probably does not arise with great frequency in the context of the biotechnology industry since virtually all companies are aware of the necessity to obtain employment agreements that require assignment of any

inventions made in the course of employment to the employer. Various states have statutory provisions which limit the scope of circumstances in which such assignment can be required, but none prevents requiring assignment where the invention was clearly made under the financial sponsorship of the employer. It is standard practice to require such agreements as a condition of employment and I am not aware of any company with any kind of financing that does not require assignment to itself of inventions made in the course of employment. If the employer owns the invention, an issue of shop right does not arise.

In the U.S., unlike other jurisdictions, inventors must be named applicants for patent protection. This requires that the inventors themselves sign the oath swearing that they are the original and first inventors of the claimed invention and that they have reviewed the application to be submitted and understand it. This does not prevent their assigning all their rights in the invention to their employer or anyone else who from then on can control the prosecution of the application to the exclusion of the inventors. The assignee cannot only control prosecution, but can further assign the invention to anyone and can disclaim all or a portion of it. Once the inventors have assigned the invention, their control over it is lost.

Even absent a written agreement that employees' inventions will be assigned to their employers, an obligation may be implied if they were actually hired to invent. This is a judicially created rule, and it appears to be most clearly applicable when the employee was specifically hired to invent what he did indeed invent.[19] This decision has been followed by many lower federal courts. It is less certain that the employer is entitled to assignment if the employee is simply generically hired to do research.[20] Several factors affect the decision, but should it be held that the employer is entitled to assignment based on the "employed to invent" principle, the issue of shop right doesn't arise either.

The shop right issue arises only when the employee retains ownership of a patent to an invention made, at least at some level, at the

19 Standard Parts Company v. Peck, 264 U.S. 52 (1924).

20 De Jur-Amsco Corp. v. Fogle, 109 USPQ 263 (3d Cir. 1956).

employer's expense. Under those circumstances, the employer is considered to have a shop right — i.e. a nonexclusive, royalty-free and nontransferable license to make and use the invention without infringing the patent. The meanings of nonexclusive, nontransferable and royalty-free are fairly clear; however, the total scope of this license is not. Clearly it extends to conducting business as usual by the employer; however, whether it will extend to business successors or expansion of the original business scope is unclear.

Trade Secrets

Trade secrets are generally protected by a mix of state statutory and judicial provisions. They comprise information that relates to the business of the trade secret holder and has been properly secured by guarding against unauthorized disclosure. There is no administrative system for obtaining protection, and it extends indefinitely, i.e. until the secret is out. In a sense, trade secret protection is the converse of patent protection; patents require full and complete disclosure of protected subject matter.

Much trade secret protection important in biotechnology is similar to that ascribable to any commercial enterprise — future business plans, future research plans, expansion or building plans, financial records and the like — having to do with the way a firm intends to conduct business, is conducting business or has conducted business. This type of trade secret may not be available to nontrade institutions such as universities and research foundations. While there appears to be no law directly on point, it may very well be that with the increased tendency of such institutions to participate in commercial development through outlicensing programs, and even equity investments in commercial enterprises, this distinction may no longer be viable.

A different type of subject matter which is also susceptible to trade secret protection overlaps that for which patent protection may be obtained. This includes ways to produce products, ways to conduct assays, particular materials useful in manufacture and even the

composition of materials that are to be sold. Protection for such things will work, of course, only if they cannot be reverse engineered (the composition discovered from analysis of products acquired in the marketplace).

The ability of its holder to keep a secret *secret* is the ultimate requirement. The holder is not protected against discovery of the trade secret because of inadequate schemes for insuring secrecy. Thus, with respect, it is necessary to initiate and maintain institutional practices which may or may not be acceptable to affected parties, such as requiring employees to sign confidentiality agreements, requiring visitors to wear badges and be escorted, requiring exit interviews for employees leaving the company, requiring identification of what is and what is not under trade secret protection and other burdensome and rather ill-defined measures to assure confidentiality.

Universities or research institutions are reluctant to institute measures which seem to contradict their presumed duty to spread knowledge. For example, even when patents are obtained, they rarely disclose every bit of knowledge needed to practice them. Thus, patents are often licensed with such "knowhow." Yet, restricting the availability of knowhow in the context of a license to a commercial enterprise may be offensive, since university researchers may feel obligated to teach the general public what they learn.

The propensity of all participants in the biotechnology industry, academic or not, to take a dim view of anything that inhibits communication with colleagues is also well known. This may diminish as industry continues to distance itself from academic environments and increases its associations with traditional pharmaceutical companies. As this occurs, the tendency of personnel involved in R&D to treat their knowledge as common property will lessen.

Patents versus Trade Secrets

Finally, patents and trade secrets should be compared. Because trade secrets do not protect against independent discovery, trying to preserve biotechnology trade secrets seems to have elevated risk factors.

Trade secret protection seems most appropriate for subject matter that is unlikely to be discovered by anyone else because it is so specific to a particular process or product that it is unlikely that a duplicate set of experiments will be conducted. Thus, it is quite inappropriate for a generic improvement that is likely to be stumbled upon by others in the field. For example, if, in the production of a particular recombinant protein, it is found that a particular fusion partner permits very high expression in a particular host organism (and the fusion partner is cleaved before the product is marketed), it may very well be that the probability of discovery by competitors is quite low. If so, trade secret protection will be fine. Yet, if it is found that a particular type of cell is extremely effective in providing large product yields for recombinant products in general, it is probably a mistake to attempt to keep it as a secret. Chances for independent discovery are great and, should independent discoverers decide to obtain a patent themselves, the trade secret holder might have to stop using its "secret" to avoid infringing their patent.

In general, then, trade secret protection for subject matter that could otherwise be patented is possible only when commercialization of the product or process or service does not automatically reveal the trade secret. It is most appropriate when the likelihood of independent discovery is vanishingly small. As that likelihood increases, a firm runs an increasing risk of not only losing its trade secret protection, but also being prevented from practicing what used to be its secret by another's patent claiming the same territory.